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     (FILE 'HOME' ENTERED AT 11:44:25 ON 30 SEP 2004)

     FILE 'CAPLUS, USPATFULL, MEDLINE, BIOSIS' ENTERED AT 11:44:57 ON 30 SEP
     2004
L1        151433 S G-PROTEIN?
L2        151433 S G PROTEIN?
L3        151433 S L1 (L) L2
L4         61729 S LUCIFERASE
L5           577 S BRET
L6           157 S L5 (L) L4
L7        151433 S L3 (L) L3
L8            78 S L3 (L) L6
L9          7745 S GPCR
L10           51 S L9 (L) L8
L11            3 S L10 AND PY <2001
L12            3 S L8 AND PY<2001
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L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
TI Detection of β2-adrenergic receptor dimerization in living cells using bioluminescence resonance energy transfer (BRET)
PY **2000**
AU Angers, Stephane; Salahpour, Ali; Joly, Eric; Hilairet, Sandrine; Chelsky, Dan; Dennis, Michael; Bouvier, Michel
SO Proceedings of the National Academy of Sciences of the United States of America (**2000**), 97(7), 3684-3689
CODEN: PNASA6; ISSN: 0027-8424
AB Heptahelical receptors that interact with heterotrimeric **G proteins** represent the largest family of proteins involved in signal transduction across biol. membranes. Although these receptors generally were believed to be monomeric entities, a growing body of evidence suggests that they may form functionally relevant dimers. However, a definitive demonstration of the existence of **G protein**-coupled receptor (**GPCR**) dimers at the surface of living cells is still lacking. Here, using bioluminescence resonance energy transfer (**BRET**), as a protein-protein interaction assay in whole cells, we unambiguously demonstrate that the human β2-adrenergic receptor (β2AR) forms constitutive homodimers when expressed in HEK-293 cells. Receptor stimulation with the hydrophilic agonist isoproterenol led to an increase in the transfer of energy between β2AR mols. genetically fused to the **BRET** donor (Renilla **luciferase**) and acceptor (green fluorescent protein), resp., indicating that the agonist interacts with receptor dimers at the cell surface. Inhibition of receptor internalization did not prevent agonist-promoted **BRET**, demonstrating that it did not result from clustering of receptors within endosomes. The notion that receptor dimers exist at the cell surface was confirmed further by the observation that BS3, a cell-impermeable crosslinking agent, increased **BRET** between β2AR mols. The selectivity of the constitutive interaction was documented by demonstrating that no **BRET** occurred between the β2AR and two other unrelated **GPCR**. In contrast, the well characterized agonist-dependent interaction between the β2AR and the regulatory protein β-arrestin could be monitored by **BRET**. Taken together, the data demonstrate that **GPCR** exist as functional dimers in vivo and that **BRET**-based assays can be used to study both constitutive and hormone-promoted selective protein-protein interactions.